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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,470	03/18/2004	Henrik Stender	58576 (48497)	7227

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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,470	STENDER ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 12, 2007 has been entered.

Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. In particular, the previous grounds of rejection under 35 USC 103 are withdrawn in view of the amendments to the claims. The following includes new grounds of rejection and is made non-final.

2. Claims 1-21 and 39 are pending and have been examined herein.

Claim Objections

3. Claims 6-11 are objected to because the assigned SEQ ID NOs have not been used to identify each sequence listed, as required under 37 CFR 1.821(d).

Maintained Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-21 and 39 are indefinite over the recitation of "wanted and unwanted." "Wanted and unwanted" are not art recognized terms to describe particular nucleic acid sequences. Because "wanted and unwanted" have not been clearly defined in the specification and because there is no art recognized definition for this term as it relates to nucleic acid sequences, one skilled in the art cannot determine the meets and bounds of the claimed invention.

Response to arguments:

In the response filed January 12, 2007, Applicants traverse this rejection by stating that there is no requirement for Applicant to provide a clear, complete and fixed definition for the phrase "wanted and unwanted." Applicants assert that the specification teaches the difference between wanted and unwanted nucleic acids and defines the

parameters of a wanted and unwanted nucleotide sequence. Applicants cite paragraphs [0027] and [0031] and Figure 1A in support of these arguments. These argument has been fully considered but is not persuasive. While the specification provides examples of what might constitute a wanted or unwanted nucleic acid, the specification does not provide a definition for this phrase. Examples of what may be encompassed by a phrase are not sufficient to provide a complete and clear definition for the phrase. As stated in MPEP 2173.05(a): "The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the

time the application is filed. Applicants need not confine themselves to the terminology used in the prior art, but are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention can be ascertained. In the present situation, because the phrases "wanted nucleic acid" and "unwanted nucleic acid" do not have a well known and accepted meaning in the prior art, in the absence of a definition for this phrase in the specification, one of skill in the art cannot determine the meets and bounds of the claimed subject matter.

Applicants assert that because the rejection under 35 USC 103 cites the patents of Heller (US Patent No. 5,532,129) and Elsas (US Patent 6,207,387) as teaching "one probe complementary to a wanted nucleic acid and the second probe is complementary to an unwanted nucleic acid sequence" that this implies that Applicants have taught what is meant by "wanted and unwanted" target sequences. This argument has also been fully considered but is not persuasive. The terms 'wanted" and "unwanted" were used within the rejection of the claims only to point out how the methods of Heller and Elsas rendered obvious the presently claimed method. Using the terms set forth in the claims within a rejection does not imply that these terms have a clear, fixed and complete definition in the art. Applicants statement that "it is impossible for the terms to be indefinite to one of skill in the art" if the terms are rendered obvious by the prior art is not persuasive. The fact that a term is indefinite and vague does not render a claim which uses that term free of the prior art. Applicants response does not provide any case law, teachings in the MPEP or other arguments to support their contention that a

claim that is rejected under 35 U.S.C. 112, second paragraph may not also be rejected under 35 U.S.C. 103.

New Grounds of Rejection:

Claims 1-21 and 39 are indefinite over the recitation of "the target sequence" (see claim 1, line 1 and step b) because it is unclear as to what is intended to be the relationship between the target sequence and the target region and between the target sequence and the wanted and unwanted DNA and RNA. For example, it is unclear as to whether the target sequence comprises the target region or is the same as the target region and/or if the target sequence is a fragment of the wanted or unwanted DNA or RNA or is the same as the wanted or unwanted DNA or RNA.

Claims 12 and 13 are indefinite over the recitation of "the binding site" because this phrase lacks proper antecedent basis. While the claim previously refers to a target region to which the probes hybridize, the claim does not previously refer to a binding site.

Claim 14 is indefinite over the recitation of "the opposite end" because this phrase lacks proper antecedent basis and because the claim does not set forth what the end is opposite to. For example, it is unclear as to whether the fluorophore is at an end opposite of the quencher or at an end opposite to that of the fluorophore of probe A, etc.

Claim 15 is indefinite over the recitation of "the two PNA probes" because this phrase lacks proper antecedent basis. While the claim previously refers to probes, the claim does not previously refer to PNA probes.

Claim 39 is indefinite over the recitation of "wherein the hybridization of probe B increases the specificity for the presence or absence of the wanted DNA or RNA sequence." While it is clear as to what is meant by the hybridization of probe B increasing the specificity of detection, it is unclear as to what is intended to be meant by hybridization increasing the specificity for the presence or absence of a nucleic acid. Further, the phrase "DNA or RNA sequence" lacks proper antecedent basis. While the claim previously refers to wanted DNA or RNA and to a target sequence, the claim does not previously refer to "wanted DNA or RNA sequence."

New Grounds of Rejection:

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 12, 16, 21 and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Schutz et al. (Clinical Chemistry. 2000. 46:1728-1737).

As set forth in paragraph 4 above, the terms "wanted" and "unwanted" DNA and RNA are not defined in the specification. Accordingly, these terms have been given their broadest reasonable interpretation as encompassing any wildtype or mutant nucleic acid sequence. The terms "wanted" and "unwanted" are used in the rejection below to clarify the relationship between the claimed invention and the method of Schutz.

Schutz (see Figures 2 and 3, page 1730 and page 1732, col. 2) teaches a method to detect target nucleic acid sequences, wherein the method comprises a) hybridizing a first probe and a second probe to a nucleic acid sample, wherein the first probe is labeled with a fluorophore (i.e., "Probe A") and the second probe is labeled with the quencher TAMRA (i.e., "Probe B"), and b) detecting the hybridization of probe A to target nucleic acid sequences under suitable hybridization conditions.

It is a property of probe A that this probe hybridizes under certain hybridization conditions, such as low stringency hybridization conditions, to both a mutated (i.e., "unwanted") and wildtype (i.e., "wanted") DNA. It is noted that the claim does not require that probe A hybridizes to both wanted and unwanted nucleic acids under any particular hybridization conditions.

It is a property of probe B that this probe hybridizes to mutant (i.e., "unwanted") DNA since this probe is an anchor probe. It is noted that the claim does not require that probe B does not hybridize with wanted nucleic acid under the hybridization conditions of the claimed method for the analysis of a target sequence. As illustrated in Figure 2 of Schutz, probe B hybridizes adjacent to the target region of probe A.

Regarding step b) of claim 1, the fluorescence generated by hybridization of probe A to mutated (unwanted) nucleic acid is quenched by hybridization of probe B (see Figure 3 and page 1732, col. 2). Further, it is a property of probe A that the presence or amount of wildtype (wanted) nucleic acid could be correlated with the fluorescence of the fluorophore of probe A since probe A also hybridizes to wildtype (wanted) nucleic acid. Note that the present claims do not require performing a positive

process step of detecting the presence or amount of wildtype (wanted) nucleic acid by detecting the fluorescence generated by hybridization of probe A alone to the wildtype (wanted) nucleic acid. Rather, the claims recite only that the method is one "wherein the presence or amount of wanted DNA or RNA present in a sample can be positively correlated with the fluorescence of the fluorophore of Probe A."

Regarding claim 5, probe A of Schutz has a length of 23 nucleotides and thereby comprises a sequence of 11-16 subunits in length (see Figure 2).

Regarding claim 12, probe A is labeled with a fluorophore at the terminus closest to the region to which probe B hybridizes, and probe B is labeled with a quencher at the terminus closest to the region to which probe A hybridizes (see Figure 2).

Regarding claim 16, Schutz teaches isolating the target nucleic acids from a cell (see page 1730, col. 1 and page 1732, col. 1).

Regarding claim 21, the detection method of Schutz allows for the diagnosis of a patients that have mutations associated with inherited deficiency of thiopurine methyltransferase, which constitutes a condition of medical of interest (see pages 1728-1729).

Regarding claim 39, the hybridization of probe B is considered to increase the specificity for the detection of the presence or absence of wanted DNA because hybridization of probe B allows for the quenching of fluorescence from probe A, thereby permitting the detection of the presence or absence of wanted DNA.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Ishibashi (U.S. Patent No. 6,872,525).

The teachings of Schutz are presented above.

Regarding claim 2, Schutz does not teach applying the method for detecting a target nucleic acid to a fluorescence in situ hybridization assay.

However, Ishibashi teaches methods for detecting nucleic acids in cells using a method of fluorescent in situ hybridization with probes labeled with FRET (fluorescence resonance energy transfer) moieties. Ishibashi (col. 4-5) teaches that the in situ hybridization method allows for the identification and separation of cells which contain specific target nucleic acid sequences.

In view of the teachings of Ishibashi, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Schutz using fluorophore and quencher labeled probes to an in situ hybridization method in order to have provided the benefit of providing a method that allowed for the detection and separation of cells based on the presence or absence of specific target nucleic acids.

7. Claims 3-4, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Nikiforov (U.S. Patent No. 6,777,184).

The teachings of Schutz are presented above.

Regarding claims 3-4 and 15, Schutz does not teach that probes A and B are high affinity probes, such as PNA probes.

However, Nikiforov (col. 24) teaches methods for detecting target nucleic acids using FRET-based probes that are PNA probes. Nikiforov teaches that PNA probes have the advantages of providing good sensitivity for SNP detection due to their large Tm differences, have a high affinity for DNA, provide fast PNA-DNA hybridization kinetics and are nuclease resistant.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Schutz so as to have used PNA probes in place of conventional DNA probes in order to have achieved the advantages set forth by Nikiforov of providing probes that increase the sensitivity and specificity of the detection of polymorphisms and mutations.

With respect to claim 15, Schutz teaches that probe A and probe B hybridize to the target nucleic acid at a distance of 14 nucleotides. Because the specification does not define what constitutes "about five nucleotide bases," the teachings of Schutz of a distance of14 nucleotides is considered to meet the limitations of the claim. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have provided probes which hybridize at a closer distance, such as a distance of 5 nucleotides, depending on the sequence of the target nucleic acid and the position of the mutation to be detected since Schutz teaches the parameters for selecting additional probes and the parameters for the selection of probes that result in quenching of fluorescent signals were well known in the art at the time the invention was made.

8. Claims 5-11 and19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Oliveira et al. (Journal of Clinical Microbiology, January 2002, Vol. 40, No. 1, pages 247-251) and Hogan.

The teachings of Schutz are presented above.

Schutz does not teach applying the detection method to the detection of a microbial sequence isolated from an microorganism treated with an antimicrobial agent and does not teach performing the detection method using probes comprising, consisting essentially of or consisting of SEQ ID NO: 1 or 2.

However, Oliveira teaches a method that distinguishes bacteria of clinical interest that are antimicrobial resistant with FISH assays that use PNA probes, wherein Oliveira's method comprises: 1) obtaining a blood sample; 2) fixing said sample and samples of reference bacterial strains to microscope slides; 3) probing all of said

samples with a *Staphylococcus aureus* (S. *aureus*) PNA probe; and 4) identifying the bacterial species in said sample with FISH. In particular, Oliveira differentiates several species bacteria. Oliveira teaches a "FISH method with peptide nucleic acid (PNA) probes for identification of *Staphylococcus aureus*...The test....is based on fluorescein-labeled PNA probe that targets a species-specific sequence of the 16S rRNA of S. *aureus*. Evaluations [were done] with 17 reference strains and 48 clinical isolates, including methicillin-resistant and methicillin-susceptible S. *aureus* species...and other clinically relevant and phylogenetically related bacteria" (abstract). Oliveira teaches that methods which distinguish between S. aureus and S. schleiferi allow one to determine the optimal antibiotic treatments for patients infected with these microorganisms.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the detection method of Schutz to the detection of microorganisms present in samples treated with antimicrobial agents in order to have provided an effective means for distinguishing between microorganisms that are methicillin-resistant and methicillin-susceptible.

With respect to claims 5-11, Oliveira teaches "fluorescein-labeled PNA probe" that comprise, consists essentially of, and consist of the instant SEQ ID NO: 1. Oliveria teaches SEQ ID NO: 1 "target[s] S. *aureus* 16S rRNA," wherein SEQ ID NO: 1 has 15 subunits in length (page 248, left column). Oliveira teaches that this nucleic acid can be used to detect S. aureus nucleic acids.

Regarding SEQ ID NO: 2, GenBank S83568 teaches a nucleic acid sequence that is the reverse complement of the instant SEQ ID NO: 2 at basepairs 83-97 (claim

limitations 7, 9, and 11). GenBank S83568 teaches that this sequence is an isolated sequence of 16S rRNA from *S. schleiferi* (definition).

Further, Hogan teaches the use of species specific PNA probes to distinguish different Staphylococcus bacteria from one another. Hogan teaches "probes, which are complementary to particular rRNA sequences of the 16S rRNA, advantageously are capable of distinguishing Staphylococcus organisms from the known phylogenetically nearest neighbors...Variable regions of rRNAs...[are] identified by comparative analysis using published rRNA sequences" wherein "commercially available software can be used" to design probes (page 12, lines 8-10 and page 14, lines 20-23). In particular, Hogan teaches that said probes can be PNA (page 18, lines 1-8).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made for the ordinary artisan to have applied the method of Schutz to the detection of S. aureus and S. schleiferi nucleic acids and to have used probes comprising, consisting essentially of or consisting of SEQ ID NO: 1 and 2 in order to have provided an effective means for distinguishing between S. aureus and S. schleiferi 16S rRNA sequences. Since the sequence of S. aureus and S. schleiferi 16S rRNA sequences were known at the time the invention was made, designing probes which could be used in the assay of Schutz, including probes of SEQ ID NO: 1 and 2, would have been obvious to one of ordinary skill in the art and well within the skill of the art at the time the invention was made. The parameters and objectives involved in the selection of probes, and particular probes that detect point mutations and which comprise fluorophores and quenchers were well known in the art at the time the

invention was made. Moreover, software programs were readily available which aid in the identification of conserved and variable sequences and in the selection of optimum probe pairs. The prior art is replete with guidance and information necessary to permit the ordinary artisan to design probes for the detection of 16S rRNA sequences from S. aureus and S. schleiferi. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the probes of SEQ ID NO: 1 and 2 in the method of Schutz in order to have provided an effective method for distinguishing between *S. aureus* nucleic acids from *S. schleiferi* nucleic acids, and thereby an effective means for distinguishing methicillin-resistant Staphylococcus bacteria from other related bacteria in order to prescribe a more appropriate, effective non-methicillin antibiotic to patients with *S. aureus* infection.

8. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Heller (U.S. Patent No. 5,532,129, published July 1996).

The teachings of Schutz are presented above. In particular, in the method of Schutz, probe B is labeled internally, while probe A is labeled at the 5' terminus (see Figure 2). Schutz does not teach a method wherein both probe A and probe B are internally labeled.

However, Heller teaches a method comprising contacting two probes with a Probe A labeled with a donor group within its 3' terminus and with a Probe B labeled with an acceptor within its 5' terminus, and wherein the probes are hybridized adjacent to one another (Figure 1B, claim limitation 12). Heller's method includes "hybridization [of the probes] to the target sequence ... the fluorescent donor group...and acceptor

group to a preselected donor-acceptor transfer distances so that when the system is irradiated by photonic energy at hv_1 the donor group absorbs the energy and transfers it...to the acceptor group which re-emits at (hv_2)," wherein Probes A and B have donor and acceptor groups respectively (column 4, lines 24-31). Heller teaches that the acceptor group is a quencher and teaches that "use of quencher chromophore (or quencher)...has the capacity to accept...the transfer of energy...but does not have significant emission (column 6, lines 63-67 through column 7, lines 1-9). Further, Heller teaches that probes A and B can be labeled internally and spacing between the donor and acceptor groups can be from 0-7 basepairs (column 10, lines 12-14 and 34-35; column 11, lines 17-19, claim limitation 13). Heller teaches that the probes can be configured in that there is "any chromophore can be paired with another chromophore to form an acceptor-donor pair, so long as the two chromophores have different emission spectrums," wherein the choromphores are defined as either fluorophores or quenchers (column 7, lines 2-11 and 32-34).

Accordingly, modification of the method of Schutz so as to have internally labeled both probe A and B would have been obvious to one of ordinary skill in the art at the time the invention was made depending on the sequence of the probe and the distance between the locations of the quencher and fluorophore labels attached to the probes. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Schutz so as to have internally labeled both probe A and probe B in order to have provided an equally effective means for detecting the presence of a mutation in TPMT nucleic acids.

9. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Meade.

The teachings of Schutz are presented above. Schutz does not teach labeling probe B with a fluorophore at the end opposite of that to which the quencher is attached, wherein the fluorophore has a different emission spectrum than the fluorophore of probe A.

However, Meade et al teaches probes that have an acceptor at their 5' terminus and a donor at their 3' terminus (Figures 1_B, D, F and H). Meade teaches "single stranded nucleic acids with at least one...donor moiety and one...acceptor moiety which hybridize to regions with exact matches can be used as controls for the presence of the target sequence" (page 11, left column, paragraph 0123). Further, Schutz does teach probes comprising two fluorophores and teaches that probes labeled with that have different emission spectrum can be distinguished from one another and used to separately detect hybridization of such probes to target nucleic acids (see page 1731 and Figure 2).

Accordingly, it would have been prima facie obvious at the time the invention was made for the person of ordinary skill in the art to have modified the method of Schutz so as to have labeled probe B at the 5' terminus with a fluorophore and at the 3' terminus with a quencher as taught by Meade. The ordinary artisan at the time the invention was made would have been motivated to have done so in order to have provided a means for distinguishing between nucleic acids to which only probe B hybridized, as compared to nucleic acids to which both probe A and probe B hybridized or probe A alone

hybridized since the fluorophores on each probe would have a different emission spectrum.

10. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schutz in view of Wohlgemuth (U.S. Patent No. 6,905,827).

The teachings of Schutz are presented above. Schutz does not teach treating the blood sample containing cells comprising the target nucleic acids by freezing to preserve the target nucleic acids within the cells.

However, Wohlgemuth (e.g., paragraph [0239], [0589])teaches methods for analyzing target nucleic acids using probes labeled with fluorophores and quenchers. Wohlgemuth (para [0123], 0428-0429] teaches that the nucleic acids to be analyzed may be obtained from blood cells present in frozen blood samples.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Schutz so as to have used frozen blood cell samples because this would have provided an effective and convenient means for analyzing target nucleic acids in archived/stored frozen blood samples.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Carla Myers

Art Unit 1634

CARLA J. MYERS
PRIMARY EXAMINER